REMARKS

Claims 1-3, 5-13, 16, 18-23 and 29 are pending in this application. By this Amendment, claims 30-35 are cancelled. In view of the foregoing amendments and following remarks, reconsideration and allowance are respectfully requested.

Rejections Under 35 U.S.C. §112, First Paragraph

A. Written Description

The Office Action rejects claims 1-3, 5-13, 16, 18-23 and 29-35 under the written description requirement of 35 U.S.C. §112, first paragraph. By this Amendment, claims 29-35 are cancelled, rendering the rejection moot as to those claims. As to the remaining claims, Applicant respectfully traverses the rejection.

To provide written description for a claim, the specification as originally filed must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, the inventors were in possession of the invention as claimed. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. *See, e.g., In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. Specifically, the Examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in the specification a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976).

The Office Action indicates that, "[i]n analyzing whether the written description requirement is met for genus claims, it is first [necessary to] determine whether a representative number of species have been sufficiently described." Although providing a representative number of species is one way to satisfy the written description requirement, it is not the only way. The written description requirement for a claimed genus may also be

satisfied by the disclosure of relevant, identifying characteristics. MPEP §2163-IIA3(a)(ii). In the present case, the claimed compositions are described by relevant, identifying characteristics. In particular, the claimed compositions are compositions comprising: a biodermal fraction representing 98-100% by weight of the composition, comprising at least two different biodermal constituents, each being cytocompatible with skin; and a non-biodermal fraction representing 0-2% by weight of the composition, comprising at least one non-biodermal constituent that is compatible with skin, wherein, if water is one of the constituents, it represents a minor part by weight of the composition.

Unlike the situation in *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), where the DNA was identified by its function, when a genus is described by relevant, identifying characteristics, there is no requirement that the specification also provide a representative number of species. However, given the predictability in this art, it is also respectfully submitted that the examples provided clearly constitute a representative number of species to support genus claims. In particular, it is respectfully submitted that the examples provided clearly demonstrate that the inventors were in possession of the necessary common attributes or features of the elements possessed by the members of the genus.

For at least the reasons set forth above, the specification clearly provides written description for the present claims. Therefore, the written description rejection should be reconsidered and withdrawn.

B. Enablement

The Office Action rejects claims 1-3, 5-13, 16, 18-23 and 29-35 under the enablement requirement of 35 U.S.C. §112, first paragraph. By this Amendment, claims 29-35 are cancelled, rendering the rejection moot as to those claims. As to the remaining claims, Applicant respectfully traverses the rejection.

Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether the disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In order to make an enablement rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided by the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). As stated by the court:

> It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosures.

In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).

Independent claim 1 is each directed to a cosmetic or dermo-therapeutic composition for a direct application onto surface parts of the human body, in a form adapted for the direct application, the composition comprising: a biodermal fraction representing 98-100% by weight of the composition, comprising at least two different biodermal constituents, each being cytocompatible with skin; and a non-biodermal fraction representing 0-2% by weight of the composition, comprising at least one non-biodermal constituent that is compatible with skin, wherein, if water is one of the constituents, it represents a minor part by weight of the composition.

Although these claims broadly define the invention, the breadth of the claims is only one factor in determining whether any needed experimentation is undue. Other factors include: the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the

existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

As pointed out in the Office Action, the specification does give examples of cosmetics that are encompassed by the claims. Although the claims are clearly broader than these examples, it is respectfully submitted that these examples, together with the knowledge of one of ordinary skill in the art, provide sufficient guidance for one of ordinary skill in the art to practice the full scope of the claims, particularly in view of the low-tech nature of this invention. The Office Action overstates the complexity related to formulating a cosmetic composition, and understates the ability of one of ordinary skill in the art to create such formulations. While many parameters may be manipulated in formulating a cosmetic composition, to say that one of ordinary skill in the art could not easily create a cosmetic composition meeting the limitations of the instant claims relying on the instant specification is simply without basis. The artisan of ordinary skill can perform numerous trivial tests and routine procedures, which, in concert with the instant specification, would readily enable him to prepare compositions and discern whether those compositions meet the limitations of the instant claims.

Moreover, the Office Action appears to infer that the instant specification must provide specific guidance as to the texture, viscosity, skin-feel, stability, fragrance and color in order to provide enablement for the instant claims. The instant claims are not limited to any particular combination of these properties -- either by composition or by function. It is well within the ability of a skilled artisan to manipulate these enumerated properties for any number of reasons bearing no relation to whether a composition is a "cosmetic composition," including, for example, attempting to ensure commercially success. The instant specification provides ample guidance to make compositions meeting the requirements of the instant

claims. Nothing more is required by the enablement requirement of 35 U.S.C. §112, first paragraph.

For at least the reasons discussed above, one of ordinary skill in the art would have been able the practice the present invention without undue experimentation. Therefore, the enablement rejection should be reconsidered and withdrawn.

Rejection Under 35 U.S.C. §102

The Office Action rejects claims 1-3, 5-8, 12, 16, 18-23 and 29-35 under 35 U.S.C. §102(b) over U.S. Patent No. 5,382,431 to Pickart ("Pickart"). By this Amendment, claims 29-35 are cancelled, rendering the rejection moot as to those claims. As to the remaining claims, Applicant respectfully traverses the rejection.

Claim 1 recites "[a] cosmetic or dermo-therapeutic composition for a direct application onto surface parts of the human body, in a form adapted for said direct application, said composition comprising: a biodermal fraction representing 98-100% by weight of the composition, comprising at least two different biodermal constituents, each being cytocompatible with skin; and a non-biodermal fraction representing 0-2% by weight of the composition, comprising at least one non-biodermal constituent that is compatible with skin, said composition having no excipient or vehicle adapted to said form of the composition, wherein, if water is one of the constituents, it is part of the biodermal fraction and represents a minor part by weight of said composition" (emphasis added). Pickart does not teach or suggest such a composition.

The Office Action asserts that Pickart discloses a composition for application to the skin including as an active ingredient a digest of collagen and/or elastin in combination with minerals such as copper and zinc. The Office Action further asserts that the compositions of Pickart may also include stearic acid or squalene. Notwithstanding these assertions, Pickart does not anticipate and would not have rendered obvious the composition of claim 1.

Claim 1 requires 98-100% by weight of a biodermal fraction including at least two different biodermal constituents that are cytocompatible with skin. As defined in the instant specification, the term "biodermal constituent" means any component or product forming part of the composition of the skin. *See* instant specification, page 4, lines 31 to 33. The active ingredient of Pickart (peptone-metal complexes -- *see, e.g.,* column 4, lines 63 to 52) relied on by the Office Action is not a "biodermal constituent," as defined in the instant application. A peptone is an artificial composition made by conducting enzymatic hydrolysis on proteins (such as elastin and collagen). The resulting product includes individual peptides obtained by artificial cleavage of the original proteins. The constituents of the artificial product cannot be found in an isolated state in the skin. That is, although precursor proteins such as elastin and collagen may be "biodermal constituents," or components forming part of the composition of the skin, their enzymatic digests and metal complexes including those digests are not.

The Office Action asserts that Pickart's disclosure of carriers such as stearic acid or squalene would constitute a second biodermal constituent within the meaning of claim 1. At the outset, Pickart does not disclose squalene; rather, Pickart discloses squalane. *See* Pickart, column 6, line 64. Squalane is not a biodermal constituent, but an artificial product obtained by complete hydrogenation of squalene. *See* excerpt from Merck Index attached hereto as "Exhibit A." As for the disclosure of stearic acid in Pickart (*see* column 6, line 65), stearic acid is disclosed as a carrier. The composition of claim 1 includes "no excipient or vehicle." Moreover, even if Pickart's disclosure of employing stearic acid could be construed as disclosure of a biodermal constitutent, there is no teaching or suggestion in Pickart of employing two different biodermal constituents in a cosmetic or dermo-therapeutic composition, much less in the claimed amount.

As Pickart fails to teach or suggest a cosmetic or dermo-therapeutic composition including 98-100% by weight of a biodermal fraction including at least two different

biodermal constituents that are cytocompatible with skin, Pickart fails to teach or suggest each and every feature of claim 1.

Claim 1 is not anticipated by Pickart. Claims 2, 3, 5-8, 12, 16, 18-23 and 29 depend from claim 1 and, thus, also are not anticipated by Pickart. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. §103

The Office Action rejects claims 1-3, 5-13, 16, 18-23 and 29-35 under 35 U.S.C. §103(a) over the Abstract of JP-63-141908 ("JP 908") in view of U.S. Patent No. 5,547,677 to Wright ("Wright") and U.S. Patent No. 5,310,556 to Ziegler ("Ziegler"). By this Amendment, claims 29-35 are cancelled, rendering the rejection moot as to those claims. As to the remaining claims, Applicant respectfully traverses the rejection.

Claim 1 is set forth above. JP 908, Wright and Ziegler do not teach or suggest such a composition.

The Office Action asserts that JP 908 discloses a composition including 0.2 to 5.0% ceramide, 0.05 to 2.0% carboxyvinyl polymer, 2.0 to 7.0% surfactant, and 10 to 70% oily substance. The Office Action asserts that it would have been obvious to incorporate squalene as taught by Wright and lecithin and cholesterol as taught by Ziegler in the composition of JP 908. Notwithstanding these assertions, JP 908, Wright and Ziegler would not have rendered obvious the composition of claim 1.

As indicated above, claim 1 requires 98-100% by weight of a biodermal fraction including at least two different biodermal constituents that are cytocompatible with skin. JP 908 does not remotely teach or suggest a composition having a biodermal fraction including two different biodermal constituents in an amount of 98-100% by weight. The Office Action asserts that it would have been obvious to include squalene as disclosed in Wright (*see* column 3, lines 53 to 59) as the "oily substance" in JP 908. However, there is no teaching or suggestion in either JP 908 or Wright to do so. JP 908 broadly discloses a composition

including an oily substance (*see* Abstract), and Wright teaches that squalene could be a desirable portion of an oil phase in an antimicrobial emulsion including an amphiphile such as glycerol monooleate, glycerol trioleate, glycerol monolaurate or glycerol dilaurate (*see* column 2, lines 12 to 24). There is nothing in either reference to suggest that the oil components disclosed in Wright to form an antimicrobial emulsion could or should be used in the composition of JP 908, which includes glucosylceramides and/or ceramides.

The Office Action further asserts that it would have been obvious to include lecithin and/or cholesterol as disclosed in Ziegler (*see* column 5, lines 62 to 66) as the "surfactant" in JP 908. However, again, there is no teaching in either JP 908 or Ziegler to do so. JP 908 broadly discloses a composition including a surfactant (*see* Abstract), and Ziegler teaches that lecithin and/or cholesterol could be a desirable component in an emulsion including petroleum jelly, sterol, phosphatide, and a C_{16} to C_{22} alkanoic triglyceride (*see* column 1, line 65 to column 4, line 5). There is nothing in either reference to suggest that the oil components disclosed in Ziegler could or should be used in the composition of JP 908, which includes glucosylceramides and/or ceramides.

Moreover, even if JP 908 were modified as suggested in the Office Action to include the squalene of Wright and the lecithin and/or cholesterol of Ziegler, the resulting composition would not include 98-100% by weight of a biodermal fraction including at least two different biodermal constituents that are cytocompatible with skin. At most, the modified composition would include 5.0% ceramide, 2.0% carboxyvinyl polymer, 7.0% lecithin and/or cholesterol, and 70% squalene. Taking a most generous view of what constitutes a biodermal consitutent, the modified composition would include 82% by weight of a biodermal fraction -- not the 98-100% by weight required by claim 1. Accordingly, even if combined as proposed in the Office Action, JP 908, Wright and Ziegler do not teach or suggest the composition of claim 1.

The Office Action appears to pick and choose individual components from disparate references to form the basis of the obviousness rejection. Applicant submits that the only teaching or suggestion to include 98-100% by weight of a biodermal fraction including at least two different biodermal constituents in a cosmetic or dermo-therapeutic composition is found in the instant specification. It is impermissible hindsight to rely on the disclosure of an application for motivation to combine the references cited against that application in a prior art rejection. *See, e.g.,* MPEP §2143 ("The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure") (citing *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991)).

As JP 908, Wright and Ziegler fail to teach or suggest a cosmetic or dermo-therapeutic composition including 98-100% by weight of a biodermal fraction including at least two different biodermal constituents that are cytocompatible with skin, the combination of references fails to teach or suggest each and every feature of claim 1.

Claim 1 would not have been rendered obvious by JP 908, Wright and Ziegler. Claims 2, 3, 5-8, 12, 16, 18-23 and 29 depend from claim 1 and, thus, would not have been rendered obvious by JP 908, Wright and Ziegler. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1-3, 5-13, 16, 18-23 and 29 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

William P. Berridge
Registration No. 30,024

Jacob A. Doughty
Registration No. 46,671

WPB:JAD/hs

Attachment:
Exhibit A

Date: June 12, 2006

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461

cyclo–Hiv–Val–MeLeu–Hiv–D-Val–D-Leu

Sporidesmolide I

Hiv = α-hydroxyisovaline

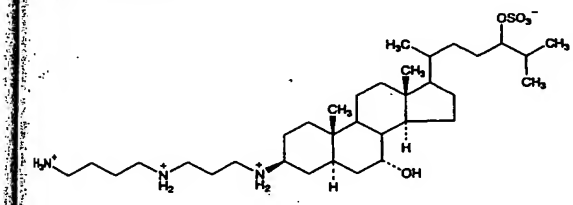
Sporidesmolide I. $C_{33}H_{58}N_4O_8$. Structure: D. W. Russell, *J. Chem. Soc.* **1962**, 753. Synthesis: M. M. Shemyakin *et al., Tetrahedron* **19**, 995 (1963). Biosynthetic study: D. W. Russell, *Biochim. Biophys. Acta* **261**, 469 (1972). MS determn: B. C. Das *et al., J. Antibiot.* **32**, 569 (1979). Needles from 70% acetic acid , mp 261-263°. $[\alpha]_D^7$ −217° (c = 1.5 in chloroform). Practically insol in water; very sol in chloroform; sparingly sol in other common organic solvents.

Sporidesmolide II. $C_{34}H_{60}N_4O_8$. *2-D-Alloisoleucine sporidesmolide I.* Structure and synthesis: M. M. Shemyakin *et al., Tetrahedron Lett.* **1963**, 1927. Crystals, mp 228-230°. $[\alpha]_D^{20}$ −195° (c = 0.6 in chloroform).

Sporidesmolide III. $C_{32}H_{56}N_4O_8$. *6-L-Leucine sporidesmolide I.* Synthesis: Y. A. Ovchinnikov *et al., ibid.* **1965**, 1111. Crystals, mp 277-278°. $[\alpha]_D$ −80° (c = 1.6 in acetic acid).

Sporidesmolide IV. $C_{34}H_{60}N_4O_8$. *4-(4-Methyl-L-2-hydroxypentanoic acid) sporidesmolide I.* Structure and synthesis: A. A. Kiryushkin *et al., ibid.* **1965**, 143; E. Bishop, D. W. Russell, *J. Chem. Soc. (C)* **1967**, 634. Crystals, mp 227-228°. $[\alpha]_D$ −195° (c = 1 in chloroform). Practically insol in water, sol in chloroform, moderately sol in common organic solvents.

8922. Squalamine. *(3β,5α,7α)-3-[[3-((4-Aminobutyl)-amino)propyl]amino]-cholestane-7,24-diol 24-hydrogen sulfate;* 3β-(*N*-[3-aminopropyl]-1,4-butanediamine)-7α,24ξ-dihydroxy-5α-cholestane 24-sulfate; 3β-*N*-1-[*N*-[3-(4-aminobutyl)]-1,3-diaminopropane]-7α,24ξ-dihydroxy-5α-cholestane 24-sulfate. $C_{34}H_{67}N_3O_5S$; mol wt 629.99. C 64.82%, H 10.72%, N 6.67%, O 12.70%, S 5.09%. Broad-spectrum aminosterol antibiotic present in shark tissues; novel indication for steroid as vertebrate host-defense agent. Isoln from the stomach of the spiny dogfish shark, *Squalus acanthias:* M. Zasloff *et al.*, U.S. pat. 5,192,756 (1993 to Children's Hospital of Penn.). Structural determn and antimicrobial activity: K. S. Moore *et al., Proc. Nat. Acad. Sci. USA* **90**, 1354 (1993). NMR spectral studies: S. L. Wehrli *et al., Steroids* **58**, 370 (1993). Synthesis of trihydrochloride: R. M. Moriarty *et al.*, PCT Int. pat. Appl. 19,366 (1994 to Magainin Pharm.).



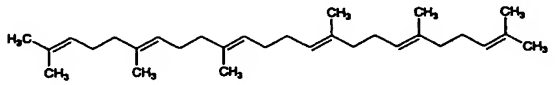
Sol in water.

8923. Squalane. *2,6,10,15,19,23-Hexamethyltetracosane;* perhydrosqualene; dodecahydrosqualene; spinacane; Cosbiol; Robane. $C_{30}H_{62}$; mol wt 422.82. C 85.22%, H 14.78%. $[(CH_3)_2CHCH_2CH_2CH_2CH(CH_3)CH_2CH_2CH_2CH(CH_3)CH_2CH_2—]_2$. Prepn by complete hydrogenation of squalene, *q.v.*: Chapman, *J. Chem. Soc.* **123**, 770 (1923); Heilbron *et al., ibid.* **1926**, 3135. Commercial grades are obtained by direct hydrogenation of shark liver oil and may contain some batyl alcohol: Tsujimoto, *Chem. Umschau Fette* **34**, 256 (1927), *C.A.* **21**, 4081 (1927). Synthesis: J. W. Scott, D. Valentine, *Org. Prep. Proced. Int.* **12**, 7 (1980); T. Mandai *et al., Tetrahedron Letters* **22**, 763 (1981).

Oil. Stable to air and oxygen. d_{15}^{15} 0.8115. mp ~−38°. bp_{760} ~350°; bp_{10} 263°; bp_5 248°. Flash pt 425°F (218°C). n_D^{15} 1.4530. Specific heat at 20° ~0.62. Viscosity (Engler) at 20° ~6.08. Readily sol in ether, gasoline, petr ether, benzene, chloroform, oils. Slightly sol in methanol, ethanol, acetone, glacial acetic acid. Concd H_2SO_4 at 70° is discolored, but the squalane remains unchanged.

USE: Lubricant, transformer oil. Ingredient of watch and chronometer oils. Perfume fixative. In pharmacy and cosmetics as skin lubricant, ingredient of suppositories, carrier of lipid-soluble drugs.

8924. Squalene. *(all-E)-2,6,10,15,19,23-Hexamethyl-2,6,10,14,18,22-tetracosahexaene;* Spinacene; Supraene. $C_{30}H_{50}$; mol wt 410.73. C 87.73%, H 12.27%. All *trans* isoprenoid contg six isoprene units. Found in large quantities in shark liver oil. Occurs in smaller amounts (0.1 to 0.7%) in olive oil, wheat germ oil, rice bran oil, and yeast. Intermediate in biosynthesis of cholesterol. Isoln: Heilbron *et al., J. Chem. Soc.* **1926**, 1630. Structure: *eidem, ibid.* **1929**, 873; Heilbron, Thompson, *ibid.* 883; Karrer *et al., Helv. Chim. Acta* **13**, 1084 (1930); Karrer, Helfenstein, *ibid.* **14**, 78 (1931); Karrer *et al., ibid.* 435. Crystal structure: J. Ernst *et al., Angew. Chem. Int. Ed.* **15**, 778 (1976). Synthesis: Trippett, *Chem. & Ind. (London)* **1956**, 80; Dicker, Whiting, *J. Chem. Soc.* **1958**, 1994; Cornforth *et al., ibid.* **1959**, 2539; Johnson *et al., J. Am. Chem. Soc.* **92**, 741 (1970); Hirai *et al., Tetrahedron Letters* **1971**, 4359; P. A. Grieco, Y. Masaki, *J. Org. Chem.* **39**, 2135 (1974). Synthesis of squalene and *trans-cis-trans-trans* isomer: Biellmann, Ducep, *Tetrahedron* **27**, 5861 (1971).



Oil. Faint, agreeable odor. Absorbs oxygen and becomes viscous like linseed oil. d_4^{20} 0.8584; bp_{25} 285°; bp_2 240°; $bp_{0.15}$ 203°. mp ~−75°. n_D^{20} 1.4965. Viscosity at 25°: 12 cps. Iodine no. 360-380. Flash pt ~200°. Practically insol in water. Freely sol in ether, petr ether, CCl_4, acetone, other fat solvents; sparingly sol in alc, glacial acetic acid.

USE: Bactericide; intermediate in manuf of pharmaceuticals, organic coloring materials, rubber chemicals, aromatics and surface active agents.

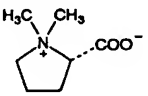
8925. Squill. Sea onion; Bulbus Scillae; Meerzwiebel. The fleshy inner bulb scales of the white variety of *Urginea maritima* (L.) Baker (*Scilla maritima* L.), *Liliaceae. Habit.* Lands of the Mediterranean seacoast. *Constit.* Glucoscillaren A (scillarenin + rhamnose + glucose + glucose); scillaren A (scillarenin + rhamnose + glucose); proscillaridin A (scillarenin + rhamnose); scillaridin A; scilliglaucoside; scillipheoside; glucoscillipheoside; scillicyanoside; scillicoeloside; scilliazuroside; scillicryptoside. *Review:* G. Baumgarten, W. Förster, *Die Herzwirksamen Glykoside* (Thieme, Leipzig, 1963) pp 70-75 *et passim.*

USE: Rodenticide.

THERAP CAT: Diuretic, emetic, expectorant, cardiotonic.

THERAP CAT (VET): Has been used as expectorant, emetic.

8926. Stachydrine. *(S)-2-Carboxy-1,1-dimethylpyrrolidinium inner salt;* methyl hygrate betaine; hygric acid methylbetaine. $C_7H_{13}NO_2$; mol wt 143.19. C 58.72%, H 9.15%, N 9.78%, O 22.35%. Occurs widely in nature, especially in alfalfa, chrysanthemum, citrus and stachys species. May be prepd by methylation of proline. Isoln: Planta, Schulze, *Ber.* **26**, 939 (1893); Jahns, *ibid.* **29**, 2065 (1896); Yoshimura, *Z. Physiol. Chem.* **88**, 334 (1913); Vickery, *J. Biol. Chem.* **61**, 117 (1924). Structure: Schulze, Trier, *Z. Physiol. Chem.* **67**, 59 (1910). Synthesis: Karrer, Widmer, *Helv. Chim. Acta* **8**, 364 (1925). Biosynthesis: Robertson, Marion, *Can. J. Chem.* **38**, 396 (1960). *Review:* Marion in *The Alkaloids* vol. 1, R. H. F. Manske, H. L. Holmes, Eds. (Academic Press, New York, 1950) pp 101-103.



Monohydrate, deliquescent crystals, sweetish taste, mp 235° when anhydr. Isomerizes at the mp to methyl hygrate. Sol in water, alcohol, dil acids. Practically insol in ether, chloroform.